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EXAMINER	
TREYGER, ILYA Y	
ART UNIT	PAPER NUMBER
3761	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,300	FOSSEL, ERIC THOR	
	Examiner	Art Unit	
	ILYA Y. TREYGER	3761	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1,5,6,11,13,17,18 and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,7-10,12,14-16,19-23 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/06/2010; 08/27/2010; 09/24/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/06/2010 has been entered.

2. Claim 4 is amended.

3. Claims 1, 5, 6, 11, 13, 17, 18 and 24-26 are canceled.

4. Claims 2-4, 7-10, 12, 14-16, 19-23, and 27-29 are examined on the merits.

Response to Arguments

5. Applicant's arguments filed 08/06/2010 have been fully considered but they are not persuasive:

6. With respect to claims 4, 20 and 29, Applicant argues that the combination of references is improper because Falk does not teach applying the medication to the breast but instead teaches applying the medication to the skin.

However, since Applicant claims applying the medication to the skin covering the breast that is a selected area of skin, the combination is deemed to be proper.

7. Applicant further argues that the combination of references is improper because Falk does not teach applying a cream to the breast, but instead teaches applying a cream to a portion of the skin where there is cancer that has metastasized from the breast.

8. However, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The reference of Falk has been brought here not for bodily incorporation of Falk's method of treatment the particular disease into the method of Fossel, but as a teaching that it is known to apply the medication into the skin by s rubbing, and therefore, the combination is deemed to be proper.

9. With respect to claim 16, Applicant's arguments are substantially identical to arguments discussed above.

Claim Objections

10. Claim 19 is objected to for improper dependency on claim 20. For examination purposes claim 19 is considered as being dependent on claim 16.

11. Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 12 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 12 is indefinite due to relative term "at least about", since there was nothing in the specification to provide any indication as to what range of specific activity is covered by the term "about." Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991).

15. Claim 16 recites the limitation "the nitric oxide donor comprises one or more of a polysaccharide-bound nitric oxide-nucleophile adduct, a N-nitroso-N- substituted hydroxylarnines, a compound containing a sulfhydryl group and a NO donor group, 1 ,3-(nitrooxymethy1)phenyl-2-hydroxybe~e, a gel comprising a nitrite salt and an acid, S-nitrosothiols, a nitrite, a 2-hydroxy-2-nitrosohydrazine, a substrate for nitric oxide synthase, a cytokine, an adenosine, bradykinin, calreticulin, bisacodyl, phenolphthalein, or endothelei" in page 3, lines 16-20; page 4, lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

16. Claim 16 is indefinite because being dependent of claim 4 recites a number of nitric oxide donors excluding L- arginine while the parent claim 4 does not recite the nitric oxide donor as a genus, but only specie of L-arginine.

17. **Claim 16 is rejected under 35 USC 112 4th paragraph, as being an improper dependent claim for failing to include all the limitations of the claim upon which it**

depends and for failing to further limit the subject matter of the claim upon which it depends.

18. Specifically, claim 16 being dependent of claim 4 recites a number of nitric oxide donors excluding L- arginine while the parent claim 4 does not recite the nitric oxide donor as a genus, but only specie of L-arginine.

As the Federal Circuit treats non-compliance with 35 USC 112 4th paragraph as a patentability issue, it is considered more appropriate to treat a claim that does not comply with 35 USC 112 4th paragraph by rejecting the claim under 35 USC 112 4th rather than by objecting to such claim under 37 CFR 1.75(c) as provided for in MPEP 608.01(n)(II). See *Pfizer Inc. v. Ranbaxy Labs., Ltd.*, 457 F.3d 1284, 1291-92 (Fed. Cir. 2006).

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. Claims 3, 4, 7-10, 12, 14, 15, 19-23 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel (US 2003/0028169) in view of Falk et al. (US 5,824,658).

22. In Re claims 4 and 29, Fossel discloses the method comprising an act of:

applying a base cream which is a delivery vehicle (P. 1, [0015], ln. 1-2) comprising a L-arginine which is a nitric oxide donor (P. 1, [0015], ln. 3) to the selected area of skin (P. 3, [0032], lines 5, 6) fully capable of being applied to the breast, since the skin covering the breast is a selected area of skin, wherein the delivery vehicle comprises a hostile biophysical environment (Abstract, lines 4-6) containing a sodium chloride (P. 1, [0010], line 3), which is a penetrating agent, and wherein the effective concentration of L-arginine is 12.5% (P. 1, [0015], ln. 3) what encompasses "at least 5%" as claimed.

With regard to limitation "for a period of time sufficient to reduce sagging", it is noted that time sufficient to reduce sagging is both indefinite and subjective, i.e. differs from patient to patient depending on number of factors, such as age, collagen content of the skin, particular clinical condition of the skin, etc., and therefore any adventives is necessarily to be applied for a period of time sufficient for providing the desired effect. Fossel does not expressly disclose the method comprising rubbing the delivery vehicle into the breast.

Falk teaches the method of treating the skin by rubbing a gel or cream by rubbing into the skin (col. 12, lines 12-15).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Fossel the step of rubbing a cream into the skin, as taught by Falk in order to improve therapeutic effect to the treatment

(Falk, col. 12, line 16) and increase absorption of the cream caused by increasing the friction that in its turn increases the area of contact of cream with the skin, and thus improves absorbtion and penetration.

23. In Re claims 3 and 19, Fossel discloses the method wherein the delivery vehicle is a cream (P. 1, [0015], ln. 1-2), wherein for examination purposes claim 19 is considering of being dependent on claim 16.

24. In Re claim 7, Fossel discloses the method wherein the effective concentration of L-arginine is 12.5% (P. 1, [0015], ln. 3) what reads on "at least 5%" as claimed.

25. In Re claims 8 and 21, Fossel discloses the method wherein the delivery vehicle comprises the water or the oil (P. 1, [0015], ln. 7).

26. In Re claims 9 and 22, Fossel discloses the method fully capable to be repeatable (P. 1, [0015], ln. 1-3).

27. In Re claim 10, Fossel discloses the claimed invention discussed above, as applied to claim 9, but does not expressly disclose the method comprising repeating the act of reapplying the delivery vehicle to the region of skin between 2 and 30 times, inclusively, within a time period of about 30 days.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use claimed time range and overall duration of treatment, since the overall duration of the medical treatment by local action compositions and the rate of application of said compositions depend of the type of skin disease, degree of the skin lesion, and degree of the positive reaction of the patient, and therefore is the matter of routine

experimentation what lies within the routine skill in the art. *In re Aller,* 105 USPQ 233(**MPEP 2144.05 (II-A)**).

28. In Re claim 12, since Fossel discloses the concentration of nitic oxide donor L-arginine of 12.5% (P. 1, [0015], ln. 3) as claimed, this amount of arginine being within the claimed range is fully capable of producing the claimed function, i. e. act for at least about 3 hours, as per claim 12.

29. In Re claim 14, 15, 27, and 28, Fossel discloses the method wherein the ionic salt comprises sodium chloride, magnesium chloride, or choline chloride (P. 1, [0015], ln. 4-7), and their combined amount is 10% as per claims 15 and 28.

30. In Re claim 20, Fossel discloses the method comprising an act of: applying a base cream which is a delivery vehicle (P. 1, [0015], ln. 1-2) comprising a L-arginine which is a nitric oxide donor (P. 1, [0015], ln. 3) to the selected area of skin (P. 3, [0032], lines 5, 6) fully capable of being applied to the breast, since the breast is a selected area of skin, for a period of time sufficient for treatment fully capable for sagging skin treatment, wherein the delivery vehicle comprises a hostile biophysical environment (Abstract, lines 4-6) containing a sodium chloride (P. 1, [0010], line 3), which is a penetrating agent, and wherein the effective concentration of L-arginine is 12.5% (P. 1, [0015], ln. 3) what encompasses "at least 5%" as claimed.

With regard to limitation "for a period of time sufficient to produce a smoother surface of the breast", it is noted that time sufficient to reduce sagging is both indefinite and subjective, i.e. differs from patient to patient depending on number of factors, such as age, collagen content of

the skin, particular clinical condition of the skin, etc., and therefore any adventives is necessarily to be applied for a period of time sufficient for providing the desired effect.

Fossel does not expressly disclose the method comprising rubbing the delivery vehicle into the breast.

Falk teaches the method of treating the skin by rubbing a gel or cream by rubbing into the skin (col. 12, lines 12-15).

The rationale of obviousness rejection discussed above in claim 4 is incorporated herein in its entirety.

21. In Re claim 23, Fossel discloses the claimed invention discussed above, as applied to claim 22, but does not expressly disclose the method comprising repeating the act of reapplying the delivery vehicle to the region of skin after between about 8 hours and about 48 hours after the act of applying the delivery vehicle.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use claimed time repeating range because the treatment time repeating range depends of the skin resistance level, which can vary from patient to patient, and therefore is the matter of optimization. *In re Aller,* 105 USPQ 233(**MPEP 2144.05 (II-A)**).

31. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel (US 2003/0028169) in view of Falk et al. (US 5,824,658), and further in view of Nakata et al. (US 5,332,758).

Fossel in view of Falk disclose the claimed invention discussed above, as applied to claim 4, but does not expressly disclose the method wherein the sagging is determined using viscoelasticity.

Nakata teaches that it is known to use Skin Viscoelasticity Test for skin diseases diagnostics (See Col. 17, ln. 9-43).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Fossel/ Falk with the determination of sagging skin, as taught by Nakata, because such modification would provide the most accurate diagnostic of the specific disease prior the therapeutic treatment.

32. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel (US 2003/0028169) in view of Falk et al. (US 5,824,658), and further in view of Marty (US 4,702,913). Fossel in view of Falk disclose the claimed invention discussed above, as applied to claim 4, but do not expressly disclose the method wherein the nitric oxide donor comprises one or more of a polysaccharide-bound'nitric oxide-nucleophile adduct, a N-nitroso-N-substituted hydroxylamines, a compound containing a sulphydryl group and a NO donor group, 1,3- (nitrooxymethy1)phenyl-2-hydroxybenzoate, a gel comprising a nitrite salt and an acid, S- nitrosothiols, a nitrite, a 2-hydroxy-2-nitrosohydrazine, a substrate for nitric oxide synthase, a cytokine, an adenosine, bradykinin, calreticulin, bisacodyl, phenolphthalein, or endothelein.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Fossel/ Falk with the use of

adenosine, as taught by Marty, because such modification would improve cosmetic or/and therapeutic effect, since adenosine promotes the release of the nitric oxide radical.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILYA Y. TREYGER whose telephone number is (571)270-3217. The examiner can normally be reached on 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tatyana Zalukaeva can be reached on 571-272-1115. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ilya Y Treyger/
Examiner, Art Unit 3761

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